

5

10

15

Transgenic animals carrying a transgene comprising a nucleic acid molecule encoding protein useful for regulating the expression of genes in eukaryotic cells and organisms in a highly controlled manner are disclosed. In the regulatory system of the invention, transcription of a *tet* operator-linked nucleotide sequence is inhibited by a transcriptional inhibitor fusion protein composed of two polypeptides, a first polypeptide which binds to *tet* operator sequences and a second polypeptide which directly or indirectly inhibits transcription in eukaryotic cells. In various embodiment, the first polypeptide binds to *tet* operator sequences either: (i) in the absence but not the presence of tetracycline (or an analogue thereof) or (ii) in the presence but not the absence of tetracycline (or an analogue thereof). In a preferred embodiment, the transgene encoding the transcriptional inhibitor fusion protein is integrated at a predetermined location within the chromosome of the transgenic animal.